CORTICOTROPHIN RELEASING FACTOR RECEPTORS ARE PRESENT ON SMALL CELL LUNG CANCER CELLS. R. Venugopal, L. Korman, M. Fagarason, A. Goldstein and T. Moody. Dept. Biochemistry and Molecular Biology, George Washington Univ. Sch. Med., Washington, D.C. 20037 and Gastroenterology Section, V.A. Med. Ctr., Washington, D.C.

Many small cell lung cancer (SCLC) cells use bombesin/gastrin releasing peptide (BN/GRP) as an autocrine growth factor. In addition to BN/GRP, several other peptides that use phosphatidyl inositol (PI) as a second messenger in SCLC cells include neurotensin, cholecystokinin, bradykinin and vasopressin. In contrast, vasoactive intestinal polypeptide (VIP) uses cyclic AMP as SCLC second messenger. Here the effects of corticotrophin releasing factor (CRF) on SCLC cells were investigated.

CRF had no effect on SCLC cell line NCI-H345 cytosolic calcium levels; the PI metabolite inositol-1,4,5-trisphosphate releases Ca^{2+} from intracellular organelles. In contrast, CRF elevated the cAMP levels in a dose dependent manner and 100 nM CRF elevated the cAMP levels 10-fold; 50 μM forskolin increased the cAMP levels 15-fold. VIPhybrid, which antagonized the increase in cAMP caused by VIP, had no effect on the cAMP increase caused by CRF. In contrast, CRF had no effect on non-SCLC cell line NCI-H838 whereas forskolin increased the cAMP levels 10-fold. Also, CRF increased secretion of BN/GRP from NCI-H345 in a dose dependent manner and 100 nM CRF increased the secretion rate by 50%. (^{125}I-Tyr^{0})CRF bound with high affinity to NCI-H345 and specific (^{125}I-Tyr^{0})CRF binding was inhibited with an IC_{50} value of 10 nM by CRF. The effects of CRF on the growth of SCLC will be discussed. These data suggest that CRF receptors are present on SCLC cells. Supported in part by NCI grant CA-53477.